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CONFERENCE REPORTS AND EXPERT PANEL

European Society of Intensive Care Medicine Clinical Practice Guideline on fluid therapy in adult critically ill patients: Part 3—fluid removal at de-escalation phase

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Abstract

Purpose: This is the third of three parts of the clinical practice guideline from the European Society of Intensive Care Medicine (ESICM) on fluid management in adult critically ill patients. This part addresses fluid removal in the de-escalation phase of shock management.

Methods: This guideline was formulated by an international panel of clinical experts, methodologists, and patient representatives. A literature search was conducted to identify relevant randomized controlled trials (RCTs) in adults published up to February 2025. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology was applied to evaluate the certainty of evidence and to move from evidence to decision.

Results: Based on data from 13 RCTs, the panel issued three conditional recommendations. The panel suggested de-escalation of fluid therapy over no de-escalation in critically ill adults after the acute phase of fluid resuscitation (low certainty evidence). They suggested protocolized fluid removal by diuretics over usual care in critically ill patients after the acute phase of fluid resuscitation (moderate certainty evidence). A conditional recommendation was issued against the routine use of ultrafiltration or extracorporeal fluid removal in critically ill adults after the acute phase of fluid resuscitation, without other indication for RRT (low certainty evidence). There was limited evidence to comment on fluid removal in specific patient cohorts.

Conclusions: This ESICM guideline provides three recommendations to inform clinicians on fluid removal during the de-escalation phase in critically ill patients with shock who no longer need fluid resuscitation.

Keywords: Fluid, Fluid removal, De-resuscitation, Diuretics, Extracorporeal fluid removal, Ultrafiltration

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The members of the "European Society of Intensive Care Medicine" are present in the electronic supplementary material 1.

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Introduction

Intravenous fluid resuscitation is a life-saving intervention in critically ill patients with shock. It is one of the most common therapeutic interventions in critical care but often contributes to a degree of fluid accumulation, especially in conditions associated with oliguria or capillary leak [1]. When the acute condition improves, most patients usually eliminate the accumulated fluids spontaneously during the recovery phase.

However, fluid accumulation may persist and contribute to harm. Moreover, sicker patients are more likely to receive larger volumes of fluid and are also more likely to die. The impact of fluid accumulation varies depending on age, comorbidity, and phase of illness but includes adverse consequences. It may induce pulmonary edema, prolonged mechanical ventilation, and development of acute kidney injury (AKI) but also delayed wound healing, tissue breakdown, and impaired bowel function with intestinal edema and intra-abdominal hypertension [2–4].

Fluid accumulation is a continuum and not defined by a specific threshold of fluid balance alone [5]. Clinicians concerned about the potential harm resulting from fluid accumulation may consider two solutions: (i) reducing/restricting the volume of fluid administered to patients, and/or (ii) actively accelerating the removal of accumulated fluid.

The European Society of Intensive Care Medicine (ESICM) convened a group of content and method experts to issue a clinical practice guideline (CPG) on fluid management in adult critically ill patients with shock. This CPG was divided into three parts: the choice of resuscitation fluids (part 1) [6], the volume of resuscitation fluids (part 2), and fluid removal in the de-escalation phase (part 3). In this manuscript, part 3 is presented. The full list of contributors is presented in the online electronic supplementary material (Supplementary file 1).

The aim of this CPG from the ESICM was to provide a concise summary of the existing evidence from clinical trials evaluating acceleration of fluid removal in critically ill patients, and to create guidance for clinical practice. In addition, the panel aimed to identify remaining uncertainties to be addressed by future research.

Methods

Guideline scope and target audience

The target population of this guideline consists of adult critically ill patients who have received and accumulated fluids and no longer require fluid resuscitation. The guideline does not apply to patients who still need active fluid resuscitation or require emergency fluid removal for life-threatening fluid accumulation. The target audience is frontline clinicians (medical, nursing, and allied healthcare workers) who care for critically ill patients.

Panel selection and organization

Panel members were appointed with consideration of diversity and inclusivity as previously described [7]. The panel consisted of two ESICM Guidelines Co-chairs (DdeB, MHM), one Clinical Chair (MO), one Methods Chair (FA), one patient representative (CJ), and 12 clinicians (AA, MC, CI, MM, XM, MN, CP, JP, ZP, OR, MSH, and AW) covering critical care, anesthesia, acute medicine, and nephrology. All panel meetings were held online.

The roles of the panel members are outlined in the online electronic supplementary material, together with the panel members of part 1 and part 2 (Supplementary file 1).

Conflict of interest management

We managed the conflict of interest (COI) as previously described [8]. Panelists were requested to declare any intellectual or financial COI that may influence their participation in the guideline by completing a special form per the ESICM procedures. A summary of individual declarations is provided at the end of the document under the COI section. Panelists received no financial incentives for their participation. In addition, no funding or input from the industry or other stakeholders was incorporated into the guideline.

Development of questions and outcomes selection

This guideline aimed to address the clinical question: In critically ill adults who no longer require fluid resuscitation, does active acceleration of fluid removal, compared to usual care, improve patient important clinical outcomes (Table 1). Before undertaking the knowledge synthesis, panel members generated a list of candidate outcomes and rated their importance to patients (1, 2, 3 = not important; 4, 5, 6 = important; 7, 8, 9 = critically important) [9] (Table 2).

Literature search

Methodologists from the University of Copenhagen, Denmark, searched Medline, EMBASE, Cochrane Central, and the WHO International Clinical Trials Registry Platform for relevant randomized-controlled trials (RCTs) in adults published up to October 31, 2022. (Supplementary File 2) An updated search was done on February 28, 2025 where one additional relevant RCT was identified.

Table 1 Guideline question and PICO

In critically ill adults who no longer require fluid resuscitation, does active acceleration of fluid removal, compared to usual care, improve patient important clinical outcomes?	
PICO	**Description**
Population	Critically ill adults who no longer require fluid resuscitation (inclusion of critically ill patients in the ICU or emergency department and patients after major surgery; exclusion of chronic dialysis patients, patients with burns or diabetic ketoacidosis, pregnant women, and non-ICU patients)
Intervention	Active acceleration of fluid removal (using diuretics and/or ultrafiltration/RRT)
Comparator	Usual care
Outcomes	1. Short-term mortality 2. Quality of life 3. Physical function (e.g., activities of daily living) 4. Cognitive function 5. ICU-free days 6. Hospital-free days 7. ventilator-free days 8. Need for RRT 9. Development of AKI
Subgroups:	
• Sepsis/septic shock	
• Acute congestive heart failure	
• Renal failure (acute/chronic)	
• Acute hypoxic respiratory failure receiving respiratory support	
• Different age groups	

AKI acute kidney injury, *ICU* intensive care unit, *RRT* renal replacement therapy

Table 2 Prioritization of outcomes

Question	Median	Minimum/maximum	Mean	Standard deviation
Short-term mortality	9.00	8.00/9.00	8.89	0.31
Quality of life (as defined in the original trials)	8.00	6.00/9.00	8.00	0.94
Functional outcomes. e.g., activities of daily living (as defined in the original trials)	8.00	5.00/9.00	7.67	1.15
Cognitive function (i.e., Extended Glasgow Outcome Scale)	8.00	3.00/8.00	6.67	1.70
ICU-free days/ICU length of stay (dependent on what is reported in the original trials)	7.00	5.00/8.00	6.78	0.92
Need for renal replacement therapy (as defined by the original trials)	7.00	3.00/9.00	6.78	1.62
Hospital-free days/hospital length of stay (dependent on what is reported in the original trials)	7.00	4.00/8.00	6.56	1.34
Ventilator-free days/duration of mechanical ventilation (dependent on what is reported in the original trials)	7.00	5.00/8.00	6.56	0.83
Acute kidney injury (as defined by the original trials)	7.00	2.00/8.00	5.89	1.97
Vasopressor-free days/duration of vasopressor therapy (dependent on what is reported in the original trials)	6.00	4.00/8.00	6.33	1.05

ICU intensive care unit

Data synthesis

We used the Dersimonian and Laird random-effects model for estimating the effect from pooled RCTs [10, 11]. We reported relative risks for dichotomous outcomes and mean differences (MDs) for continuous outcomes, both with their corresponding 95% confidence

intervals (CI). We examined heterogeneity descriptively using the I^2 [12]. All analyses were performed using Review Manager (RevMan) [Version 5.4, The Cochrane Collaboration, 2020]. We applied the principles of Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) guidance, related to magnitude of effect size and certainty of evidence [13]. The panel considered the importance of each outcome, both desirable and undesirable.

Certainty of evidence

The panel used the *Grading of Recommendations, Assessment, Development, and Evaluation* (GRADE) approach [14] to assess the certainty of evidence for each outcome GRADE [15]. Certainty of evidence was rated as high, moderate, low, or very low, based on the risk of bias of included trials [16], imprecision [17, 18], indirectness [19], inconsistency [20], and risk of publication bias [21]. The certainty of evidence for each recommendation was determined considering the totality of evidence across all outcomes including the critical outcome with the lowest certainty [22]. In addition and in line with the GRADE methodology, the panel also considered the relative importance of each outcome, so that the whole body of evidence was not downgraded because of the lower confidence in estimates of the effects of a less critical outcome.

For each PICO, we reported the level of certainty for each outcome, the level of certainty for the whole body of evidence and the domains that were involved in downgrading in the corresponding Summary of Evidence section, and provided a more detailed description in the Evidence Profile tables in Supplementary files 3. The GRADEpro GDT [GRADEpro Guideline Development Tool (Software), McMaster University and Evidence Prime, 2022. Available from www.gradepro.Org] was applied to create evidence profiles for each PICO.

Recommendation formulation

Following anonymous voting online, the Evidence-to-Decision (EtD) Framework was used to formulate recommendations [23, 24]. As outlined in the GRADE methodology, the panel considered the following factors: magnitude of effect, certainty of evidence, patient values and preferences, resources and cost, equity, acceptability, and feasibility when deciding the direction and strength of recommendations. The detailed EtD framework for each PICO is shown in Supplementary files 4, 5 and 6.

The final recommendations adhere to GRADE's recommendations for informative wording to describe the results of the pooled estimates [13]. A strong recommendation in favor of an intervention (reported as "we recommend") implies that the desirable benefit of the intervention outweighs undesirable effects, that most patients and clinicians would choose the recommendation, and that it can be adopted as a policy. On the other hand, a conditional recommendation in favor of an intervention (reported as "we suggest") implies that the desirable benefit of the intervention outweighs the undesirable effects but with a low confidence. It implies that a majority, but not all, individuals will likely be best served by the recommended course of action, and that most patients and clinicians, but not all, would accept the suggested action from a conditional recommendation. The panel used consensus to formulate recommendations; the final recommendations were approved by all members. For each PICO, the panel also identified unresolved questions and relevant research gaps.

Results

Literature search

The initial literature search revealed 19,948 articles (Supplementary file 2). Following review of the titles and abstracts, 25 articles were read in full. Thirteen RCTs (including 2549 patients) met criteria for inclusion in the meta-analysis [25–37] (Table 2). The main reasons for exclusion of 12 studies were different patient population, non-RCT study design, and secondary analyses of RCTs.

The included studies varied in the patient population, study protocols, and outcomes (Table 2). In addition, 7 studies combined fluid restriction with fluid removal and 6 studies focused only on fluid removal.

PICO 1: Should de-escalation of fluid therapy versus no de-escalation be used in critically ill patients after the acute phase of fluid resuscitation?

Recommendation

We suggest de-escalation of fluid therapy over no de-escalation in critically ill adults after the acute phase of fluid resuscitation (*conditional recommendation, low certainty evidence*)

Background: Fluid accumulation is associated with worse outcomes, including prolonged need for respiratory support, longer stay in ICU, and increased mortality [38]. While fluid accumulation may simply reflect severity of illness, there is evidence that organ edema can directly contribute to organ dysfunction and multi-organ failure and that decongestion is beneficial [4, 39–42]. The risk of worse outcomes is higher in patients with prolonged fluid accumulation and edema. However, inappropriate or overzealous fluid removal is also associated with harm from hemodynamic instability [43]. In addition, both, diuretics and ultrafiltration have side effects, including potentially life-threatening complications.

Table 3 RCTs included in meta-analysis

Study	N	ICU population	Aim of study	Intervention	Control	Outcomes (intervention vs usual care)
Chen et al. 2015 [25]	82	Septic shock deemed not to be volume responsive and requiring vasoactive therapy for at least 12 h	To investigate whether a protocol of daily fluid status assessment resulting in targeted fluid minimization could be used safely in patients with septic shock	Fluid minimization (fluid restriction, diuretics, or RRT as needed)	Usual care	In-hospital mortality (56.1% vs 48.8%; $p=0.51$) RRT (41.5% vs 39%; $p=0.82$) Ventilator days (8 vs 5 days; $p=0.30$) Vasopressor days (4 vs 4 days; $p=0.84$)
SPARK study Bagshaw et al. 2017 [26]	73	AKI and resuscitation goals achieved	To compare the efficacy and safety of continuous infusions of furosemide or placebo titrated to urine output on the incidence of worsening AKI	Furosemide loading dose of 0.4 mg/kg followed by a continuous infusion commenced at 0.05 mg/kg/h	Placebo	Worsening AKI (43.2% vs 37.1%; $p=0.6$) Kidney recovery (29.7% vs 42.9%; $p=0.3$) RRT (27.0% vs 28.6%; $p=0.8$) Hospital mortality (8.1% vs 14.3; $p=0.5$) 90-day mortality (21.6% vs 30.5%; $p=0.4$)
FFAKI trial Berthelsen et al. 2018 [27]	23	AKI and renal recovery score $\leq$ 60% and fluid accumulation of > 10% ideal body weight	To test whether forced fluid removal was feasible in critically ill patients and led to a clinically relevant difference in fluid balance compared to standard care	Forced fluid removal (furosemide infusion and/or RRT)	Usual care	RRT (14% vs 31%; NS) Duration of vasopressor use (5 vs 3 days; $p=0.54$)
IRIHS study Cinotti et al. 2021 [28]	171	Fluid accumulation of $\geq$ 3% ideal body weight and on MV and hemodynamically stable	To investigate whether the administration of diuretics could decrease the fluid balance in patients with weight gain undergoing invasive mechanical ventilation	Diuretics once or twice a day Until extubation	Usual care; diuretics only allowed as rescue therapy	ICU mortality (14% vs 18; $p=0.5$) 60-day mortality (16.9% vs 22.5%; $p=0.5$) RRT (7.8% vs 4.5%; $p=0.4$) Ventilator-free days at day 60 (54 vs 51 days; $p=0.7$)
RADAR-2 Silversides et al. 2021 [29]	180	MV and expected to stay in ICU for > 24 h	To investigate the feasibility, safety, and clinical outcomes of a strategy of conservative fluid administration and targeted fluid removal compared with usual care	Fluid restriction; diuretics/RRT if cumulative FB > 2L since ICU admission	Usual care	New AKI (4.5% vs 5.6%; $p=0.75$) 28 d mortality (21.4% vs 15.6%; $p=0.32$) Ventilator-free days (16.6 vs 17.9 days; $p=0.68$) Cognitive dysfunction at 180 d (33.3% vs 47.4%; $p=0.37$) Anxiety at 180 d (22.2% vs 46.7%; $p=0.14$) PTSD at 180 d (57.9% vs 60%; $p=0.90$)
REVERSE AKI Vaara et al. 2021 [30]	100	AKI but not on RRT and not hypovolemic	To test whether a restrictive fluid-management regimen would lead to a lower cumulative fluid balance at 72 h post-randomization	Fluid restriction and diuretics/RRT	Usual care	Days alive and free of MV (13 vs 11.5 days; $p=0.284$) 90-day mortality (19.6% vs 26.5%; $p=0.387$) RRT (13% vs 30%; $p=0.043$)

Table 3 (continued)

Study	N	ICU population	Aim of study	Intervention	Control	Outcomes (intervention vs usual care)
Cantarovich et al. 2004 [32]	338	AKI treated with RRT	To test the effect of high-dose furosemide on survival and renal recovery	Furosemide (25 mg/kg/d iv or 35 mg/kg/d orally)	Placebo	Mortality (35% vs 30.5%; $p=0.36$) Duration of RRT (11.4 vs 12.4 days; $p=0.21$)
FACTT study, ARDS Clinical Trials Network, 2006 [33]	1000	Acute lung injury	To investigate the risks and benefits of a fluid-management protocol with a lower or higher intravascular pressure (PAOP or CVP)	Conservative fluid management (fluid restriction and diuretics)	Usual care	60 d mortality (25.5% vs 28.4%; $p=0.30$) Renal failure (21.5% vs 21.2%; $p=0.59$) RRT (10% vs 14%; $p=0.06$) Ventilator-free days (14.6 vs 12.1 days; $p<0.001$)
Semler et al. 2020 [36]	30	Suspected infection and SIRS and either shock or respiratory failure	To investigate whether a conservative fluid-management protocol would decrease mean daily fluid balance and increase days alive and free of ICU compared with usual care	Conservative fluid management (fluid restriction and furosemide infusion)	Usual care	AKI III (21.4% vs 40%; $p=0.28$) RRT (6.7% vs 6.7%; $p>0.99$) Hospital mortality (30% vs 26.7%; $p>0.99$) Ventilator-free days (12 vs 13 days; $p=0.60$)
Hamishehkar et al. 2017 [34]	106	Oliguric AKI	To evaluate the effect of giving furosemide to convert oliguric to non-oliguric AKI	Furosemide bolus followed by infusion	Usual care but no diuretics	ICU mortality (20% vs 28%; $p=0.35$) 28 d mortality (20% vs 28%; $p=0.35$)
Mitchell et al. 1992 [35]	101	Pulmonary edema requiring PAC	To evaluate whether a strategy of measuring EVLW instead of WP to guide fluid management would favorably affect the development or resolution of pulmonary edema and other relevant outcomes	EVLW management: fluid restriction, diuretics ± vasopressors	WP management: vasopressors, fluids, less diuretics	Duration of MV (9 vs 22 days; $p=0.047$) Hospital mortality (56% vs 65%; $p=0.327$)
Mekontso Dessap et al. 2012 [31]	304	MV and hemodynamic stability	To test whether during the weaning period, fluid management guided by daily BNP plasma concentrations would improve outcomes compared with empirical therapy dictated by clinical acumen	BNP-guided fluid management, including fluid restriction and diuretics	Usual care	Ventilator-free days by day 28 (25.9 vs 23.3 days; $p=0.038$) Hospital mortality (13.2% vs 16.4%; $p=0.433$) 60 d mortality (13.8% vs 18.4%; $p=0.275$)

Table 3 (continued)

Study	N	ICU population	Aim of study	Intervention	Control	Outcomes (intervention vs usual care)
Wichmann et al. 2023 [37]	41	Intensive care patients with at least 5% fluid overload	To study whether fluid removal with furosemide versus placebo would increase the number of days alive and out of the hospital after 90 days	Furosemide bolus followed by furosemide infusion to achieve daily negative fluid balance	Placebo	Cumulative fluid balance on day 3: 1927 vs 5139 ml Median number of days alive and out of hospital at day 90: 50 vs 45 days (mean difference 1 day, 95% CI −19 to 21, *p*-value 0.94) 90-day mortality: 40% vs 29%; RR 1.40 (0.39–7.35); p = 0.44

AKI acute kidney injury, *BNP* B-type natriuretic peptide, *CI* confidence interval, *CVP* central venous pressure, *EVLW* extravascular lung water, *FB* fluid balance, *ICU* intensive care unit, *MV* mechanical ventilation, *RR* relative risk, *RRT* renal replacement therapy, *SIRS* systemic inflammatory response syndrome, *PAC* pulmonary artery catheter, *PAOP* pulmonary artery occlusion pressure, *WP* pulmonary capillary wedge pressure

Summary of evidence

A pooled analysis of 13 RCTs showed that protocolized de-escalation of fluid therapy compared with no active de-escalation of fluid therapy in critically ill patients resulted in little-to-no difference in mortality [relative risk (RR) 0.93, 95% CI 0.82–1.05] (Tables 3 and 4). There was no significant mortality difference when only analyzing studies that assessed active fluid removal versus usual care and excluding studies that combined fluid restriction with fluid removal (RR 0.95, 95% CI 0.72–1.25).

The mean number of ICU-free days was 2.2 days higher (1–3.3 days more) with de-escalation of fluid therapy, but certainty was low. The mean number of ventilator-free days was 1.3 days more with active fluid removal, ranging from 1.38 fewer to 4.04 more days.

The certainty of evidence of the pooled data for all other outcomes was very low and the effects of actively accelerating fluid removal on those outcomes remain highly uncertain. However, it should be pointed out that fluid targets were not always achieved in the intervention groups [29, 44]. Furthermore, the validity of most RCTs was compromised by their inability to achieve adequate fluid separation between the intervention and usual care cohorts.

There were no data available to inform any of the prespecified subgroups. It was acknowledged that subgroup analyses are typically underpowered and that this does not rule out the possibility that clinical effects may vary between specific patient groups and different clinical settings.

The panel considered additional factors when formulating recommendations for fluid removal during the de-escalation phase versus no de-escalation of fluid therapy (EtD framework). First, diuretics are available worldwide and generally affordable, whereas ultrafiltration may not be routinely available or affordable everywhere. The panel noted that there were no studies examining cost-effectiveness of fluid removal strategies. Second, the reported adverse effects were considered minor to trivial but may be higher in real life, especially with mechanical fluid removal. Regarding patient values and preferences, the panel felt that most patients would likely find fluid removal strategies acceptable, especially the use of diuretics. However, diuretics may not always be effective, for instance in patients with poor kidney function, hypoalbuminemia [45], or diuretic resistance, which may potentially prolong the duration of fluid accumulation. Regarding acceptability of RRT or ultrafiltration, a survey of 68 out of 82 eligible patients who had received RRT in the context of multi-organ failure in the ICU, revealed that 98% of patients would have chosen RRT again if given the

Table 4 Evidence profile for PICO 1 "Should de-escalation of fluid therapy versus no de-escalation be used in critically ill patients after the acute phase of fluid resuscitation?"

Outcomes	With no Deresuscitation	With Deresuscitation	Difference	Relative effect (95% CI)
Mortality	290 per 1,000	**270 per 1,000** (238 to 304)	**20 fewer per 1,000** (52 fewer to 14 more)	**RR 0.93** (0.82 to 1.05)
ICU-free Days - All	The mean iCU-free Days - All was **0** days	The mean iCU-free Days - All in the intervention group was 2.2 days more (1 more to 3.3 more)	MD **2.2 days more** (1 more to 3.3 more)	-
Ventilator-free days -all groups	The mean ventilator-free days - all groups was **0** days	The mean ventilator-free days - all groups in the intervention group was 1.33 days more (1.38 fewer to 4.04 more)	MD **1.33 days more** (1.38 fewer to 4.04 more)	-
Need for RRT - all	136 per 1,000	**111 per 1,000** (87 to 145)	**24 fewer per 1,000** (49 fewer to 10 more)	**RR 0.82** (0.64 to 1.07)
AKI-all	74 per 1,000	**58 per 1,000** (30 to 114)	**16 fewer per 1,000** (45 fewer to 39 more)	**RR 0.78** (0.40 to 1.53)
Mortality: Sensitivity analyses: excluding the studies that combined restrictive fluid administration and removal, i.e. only including studies assessing active removal (diuretics +/- RRT) vs. no removal.	288 per 1,000	**273 per 1,000** (207 to 360)	**14 fewer per 1,000** (81 fewer to 72 more)	**RR 0.95** (0.72 to 1.25)
Need for RRT: Sensitivity analyses: excluding the studies that combined restrictive fluid administration and removal, i.e. only including studies assessing active removal (diuretics +/- RRT) vs. no removal.	139 per 1,000	**148 per 1,000** (91 to 244)	**8 more per 1,000** (49 fewer to 104 more)	**RR 1.06** (0.65 to 1.75)
Mortality: Patients with fluid overload.	274 per 1,000	**255 per 1,000** (214 to 304)	**19 fewer per 1,000** (60 fewer to 30 more)	**RR 0.93** (0.78 to 1.11)
Mortality: Patients without HD instability	206 per 1,000	**173 per 1,000** (120 to 247)	**33 fewer per 1,000** (87 fewer to 41 more)	**RR 0.84** (0.58 to 1.20)
Mortality: Patients with respiratory failure	278 per 1,000	**245 per 1,000** (211 to 284)	**33 fewer per 1,000** (67 fewer to 6 more)	**RR 0.88** (0.76 to 1.02)
Mortality: Patients without respiratory failure	462 per 1,000	**286 per 1,000** (78 to 1,000)	**175 fewer per 1,000** (383 fewer to 595 more)	**RR 0.62** (0.17 to 2.29)

AKI acute kidney injury, *CI* confidence interval, *HD* hemodynamic, *ICU* intensive care unit, *RRT* renal replacement therapy, *RR* relative risk

choice again [46]. The panel acknowledged that in some countries, the costs of ultrafiltration and RRT are paid out-of-pocket, putting patients at risk of rapid impoverishment [47].

Considering all factors, the panel made a conditional recommendation in favor of fluid removal during the de-escalation phase in critically ill patients, provided that the patient no longer needs fluid resuscitation and is hemodynamically stable.

Unresolved questions and research gaps

The optimal strategy of fluid removal during the de-escalation phase (timing, type, dose and mode of diuretic therapy, mode and rate of mechanical fluid removal, combination therapy, monitoring, duration, and discontinuation) remains uncertain. The effect of active fluid removal on quality of life and physical and cognitive function is not known either. The panel acknowledged that an adjunct study to the Acute Respiratory Distress Syndrome Clinical Trials Network Fluid and Catheter Treatment Trial (FACCT) [33] had performed neuropsychological function testing in survivors at 2 and 12 months post-hospital discharge and had shown cognitive impairment in patients randomized to the conservative fluid-management strategy ($P=0.005$) [48]. Of the included RCTs, only the RADAR-2 trial included cognitive dysfunction at 180 days as an outcome and showed no significant difference between patients in the intervention and usual care arm [29]. The panel felt that further research was urgently needed.

PICO 2: Should protocolized fluid removal by diuretics versus usual care be used in critically ill patients after the acute phase of fluid resuscitation?

Recommendation

We suggest protocolized fluid removal by diuretics over usual care in critically ill patients after the acute phase of fluid resuscitation (*conditional recommendation, moderate certainty evidence*)

Background: Diuretics are often considered first-line therapy to remove excess fluid, as monotherapy or in combination using loop diuretics, carbonic anhydrase inhibitors, thiazides, thiazide-like drug classes, and mineralocorticoid receptor antagonists [49]. The goal is to increase urine output and to decrease intravascular hydrostatic pressure and reduce interstitial edema and compartmental pressures (especially in the abdomen). One of the downsides of diuretics is that the diuretic response is not predictable. Also, diuretic efficacy may decrease under certain conditions, prolonging the duration of fluid accumulation.

While diuretics are not nephrotoxic per se, excessive diuresis can also lead to fluid depletion and a fall in glomerular filtration. A multi-center prospective observational study in China concluded that diuretics accounted for 22.2% of all drug-induced AKI, ranked only after antibiotics [50]. While diuretics indeed contribute to AKI if given to patients without hypervolemia, it is important to emphasize that successful decongestion with diuretics can benefit kidney function [51]. For instance, in patients hospitalized with decompensated heart failure, successful decongestion was associated with better outcomes (hospitalization, survival) than partial decongestion even if associated with a temporary elevation of serum creatinine [52].

Summary of evidence

A pooled analysis of 10 RCTs showed that protocolized fluid removal using diuretics compared to usual care in critically ill patients resulted in little-to-no difference in mortality (RR 0.90, 95% CI 0.79–1.02) (Table 5). Similarly, there was no difference in the risk of developing AKI (RR 0.78, 95% CI 0.40–1.53) but the chance of receiving RRT was significantly lower with diuretic therapy (RR 0.72, 95% CI 0.55–0.96).

There was no significant mortality difference when excluding studies that combined fluid restriction with fluid removal (RR 0.97, 95% CI 0.73–1.28). There were also no significant mortality differences in subgroup analyses of patients with fluid accumulation [defined in respective trials as >3%, >5% or >10% increase in body weight (Table 3)], respiratory failure, sepsis or AKI.

The panel acknowledged that diuretics are available worldwide and generally affordable, but health economic data were not available. A reduction of the risk of RRT was considered important. Reported adverse effects of diuretics were considered minor to trivial but may be higher in real life. In addition, the panel emphasized that diuretics may not always be effective, potentially prolonging exposure to fluid overload.

Considering all factors, the panel made a conditional recommendation in favor of using diuretics for fluid removal in critically ill patients after the acute phase of fluid resuscitation, provided patients have sufficient kidney function to respond.

Table 5 Evidence profile for PICO 2 "Should protocolized fluid removal by diuretics versus usual care be used in critically ill patients after the acute phase of fluid resuscitation?"

Outcomes	With non-protocolised fluid removal / usual care	With protocolised fluid removal by diuretics	Difference	Relative effect (95% CI)
Mortality - DIuretics only	285 per 1,000	**256 per 1,000** (225 to 290)	**28 fewer per 1,000** (60 fewer to 6 more)	**RR 0.90** (0.79 to 1.02)
ICU-Free days	The mean iCU-Free days was **0** days	The mean iCU-Free days in the intervention group was 2.2 days more (1.09 more to 3.31 more)	MD **2.2 days more** (1.09 more to 3.31 more)	-
Ventilator-free days -diuretics	The mean ventilator-free days - diuretics was **0** days	The mean ventilator-free days - diuretics in the intervention group was 2.53 days more (1.19 more to 3.86 more)	MD **2.53 days more** (1.19 more to 3.86 more)	-
Need for RRT - diuretics	119 per 1,000	**85 per 1,000** (65 to 114)	**33 fewer per 1,000** (53 fewer to 5 fewer)	**RR 0.72** (0.55 to 0.96)
AKI - diuretics	54 per 1,000	**42 per 1,000** (21 to 82)	**12 fewer per 1,000** (32 fewer to 28 more)	**RR 0.78** (0.40 to 1.53)

AKI acute kidney injury, *CI* confidence interval, *ICU* intensive care unit, *RRT* renal replacement therapy, *RR* relative risk

Unresolved questions and research gaps

Research is needed to determine the optimal method of using diuretics in individual patient cohorts and to identify those who are unlikely to respond.

PICO 3: Should protocolized fluid removal using ultrafiltration or extracorporeal renal replacement therapy versus usual care (no ultrafiltration or extracorporeal renal replacement therapy) be used for critically ill patients after the acute phase of fluid resuscitation?

Recommendation

We suggest against the routine use of ultrafiltration or extracorporeal fluid removal in critically ill adults after the acute phase of fluid resuscitation, without other indication for RRT (*recommendation, low certainty evidence*)

Background: Mechanical fluid removal includes isolated ultrafiltration and RRT. While isolated ultrafiltration is purely intended for the removal of fluid, RRT allows removal of water, electrolytes, solutes, and exogenous waste products [53]. Compared to diuretics, RRT is invasive and represents a significant step-up in care and complexity. An important advantage of mechanical fluid removal is that the target removal rate can be controlled. However, the volume of fluid that is ultimately withdrawn is often lower than targeted. For example, in the RADAR-2 trial, an open-label RCT, 180 mechanically ventilated adult ICU patients were randomized to either a conservative fluid-management strategy, including active fluid removal if fluid accumulation was present, or usual care. While fluid removal was possible in both groups, only one-third of patients in the intervention group achieved the daily fluid balance target [29].

Further, ultrafiltration removes fluid with electrolyte concentrations similar to that of plasma, whereas diuretics remove relatively more water than sodium, so that excess sodium is left behind [54]. This combined with neurohormonal activation may explain why the initial weight loss after diuretics is rapidly negated in some patients. Finally, in case of absent kidney function, mechanical fluid removal is the only option.

The effects of mechanical fluid removal on renal function vary. Excessive ultrafiltration can lead to intravascular hypovolemia and AKI. Several observational studies in critically ill patients have also shown an association between initiation of RRT and reduction of urine output [55]. Studies in patients with decompensated congestive heart failure have reported improved renal function with decongestion that could be explained by better cardiac performance and relief of renal congestion. In contrast, other studies demonstrated a higher incidence of renal dysfunction [56, 57]. These discrepancies may be attributable to specific patient characteristics but also differences in the rate of ultrafiltration and potential imbalances between the fluid removal rate and vascular refill capability, together with variations in medical management.

Summary of evidence

A pooled analysis of 4 RCTs demonstrated no difference in mortality (RR 1.13, 95% CI 0.083–1.53) between fluid removal using ultrafiltration or RRT versus usual care (Table 6). When evaluated, there was no significant difference in ventilator-free days, quality of life, risk of cognitive dysfunction, or post-traumatic stress. There was also no significant mortality difference when excluding studies that combined fluid restriction with fluid removal (RR 0.62, 95% CI 0.17–2.29). Similarly, there was no significant mortality difference in subanalyses of patients with fluid accumulation, respiratory failure, sepsis or AKI.

The panel acknowledged that ultrafiltration and RRT may be the only potential strategy to remove fluid in patients with absent kidney function or diuretic resistance. However, the necessary devices and expertise may not be routinely available or affordable [58]. Therefore, in the absence of any clear benefit (apart from in patients with absent kidney function or diuretic resistance), the panel suggested against the routine use of ultrafiltration or extracorporeal fluid removal in critically ill adults with fluid accumulation (syndrome) after the acute phase of fluid resuscitation.

Values and preferences

The panel acknowledged that both diuretics and ultrafiltration were established therapies. Further, previous evaluations of patients who had received RRT for AKI revealed that most survivors wished to receive similar treatments again if required [59].

Quality of life, and functional and cognitive function were considered by the panel to be critically important outcomes (Table 2). Only the RADAR-2 trial included cognitive function as an outcome and showed no significant difference between patients in the intervention and usual care arm [29].

Resources and cost

No study included any cost-effectiveness analyses. The panel felt that diuretics were available worldwide and usually affordable, but costs for ultrafiltration and RRT may be a concern in some low- and middle-income countries [58].

Table 6 Evidence profile for PICO 3 "Should protocolized fluid removal using ultrafiltration or extracorporeal renal replacement therapy versus usual care (no ultrafiltration or extracorporeal renal replacement therapy) be used for critically ill patients after the acute phase of fluid resuscitation?"

Outcomes	With non-protocolised fluid removal / usual care	With protocolised fluid removal using ultrafiltration or extracorporeal renal replacement therapy	Difference	Relative effect (95% CI)
Mortality - Diuretics & RRT	331 per 1,000	**374 per 1,000** (27 to 506)	**43 more per 1,000** (304 fewer to 175 more)	**RR 1.130** (0.083 to 1.530)
QOL assessed with: EQ5D5L index	The mean QOL was **0**	The mean QOL in the intervention group was 0.1 more (0.13 fewer to 0.33 more)	MD **0.1 more** (0.13 fewer to 0.33 more)	-
QOL assessed with: EQ5D5L-VAS	The mean QOL was **0**	The mean QOL in the intervention group was 5.7 more (12.48 fewer to 23.88 more)	MD **5.7 more** (12.48 fewer to 23.88 more)	-
Cognitive dysfunction	474 per 1,000	**332 per 1,000** (156 to 720)	**142 fewer per 1,000** (317 fewer to 246 more)	**RR 0.70** (0.33 to 1.52)
Anxiety	467 per 1,000	**224 per 1,000** (79 to 616)	**243 fewer per 1,000** (387 fewer to 149 more)	**RR 0.48** (0.17 to 1.32)
Depression	500 per 1,000	**100 per 1,000** (25 to 405)	**400 fewer per 1,000** (475 fewer to 95 fewer)	**RR 0.20** (0.05 to 0.81)
PTSD	600 per 1,000	**576 per 1,000** (330 to 1,000)	**24 fewer per 1,000** (270 fewer to 420 more)	**RR 0.96** (0.55 to 1.70)
Ventilator-free days -diuretics +/-RRT	The mean ventilator-free days -diuretics +/-RRT was **0** days	The mean ventilator-free days -diuretics +/-RRT in the intervention group was 1.4 days lower (4.57 lower to 1.77 higher)	MD **1.4 days lower** (4.57 lower to 1.77 higher)	-

AKI acute kidney injury, *CI* confidence interval, *ICU* intensive care unit, *QOL* quality of life, *RRT* renal replacement therapy, *RR* relative risk

Unresolved questions and research gaps

The panel rated quality of life and cognitive function as very important outcomes after mortality, but there are almost no data in the literature regarding these important end-points.

Research is also needed to identify the optimal ultrafiltration rate in individual patients to minimize the duration of exposure to fluid accumulation without causing harm from excess fluid removal. Cost-effectiveness studies on the use of mechanic removal vs medication removal are needed.

Discussion

Data from 13 RCTs support a practice of fluid removal during the de-escalation phase over no fluid removal in critically ill adults after the acute phase of fluid resuscitation. Although there was no difference in mortality, the mean number of ICU-free days was 2.2 days higher with de-escalation of fluid therapy. The panel suggested protocolized fluid removal by diuretics over usual care and issued a conditional recommendation against the routine use of ultrafiltration or extracorporeal fluid removal in patients without other indications for RRT.

A suggestion (i.e., a weak recommendation) implies that while most people would choose the suggested intervention, some would not. The panel accepted that there were no significant mortality differences in subanalyses of patients with fluid accumulation, respiratory failure, sepsis, or AKI. However, the definitions of these important subgroups were variable. Further, subgroup analyses do not rule out the possibility that clinical effects may vary between specific patient groups and different clinical

settings. For instance, in individual patients with poor kidney function, diuretic resistance, or life-threatening fluid accumulation, ultrafiltration may be the most effective strategy to remove excess fluid and prevent harm.

The panel acknowledged the use of various different terms in the literature describing the accumulation of fluid, including hypervolemia, fluid overload, fluid excess, fluid accumulation, and fluid accumulation syndrome without objective criteria and a standardized approach to use in clinical practice [4, 5, 38, 40, 41, 54, 60–63]. In addition, a survey of 524 intensive care specialists in the UK confirmed marked practice variability in fluid management, including fluid removal [64]. The GODIF trial by Wichmann et al. showed that the use of cumulative fluid balance as the sole parameter to assess fluid overload was imprecise which resulted in the early termination of the trial [37]. We acknowledge that the terminology is heterogeneous, but it was beyond the scope of this guideline to determine objective evidence-based definitions. The panel also extensively discussed the heterogeneity of study protocols and interventions and acknowledged that the data did not allow them to differentiate between specific types of diuretics, combination therapies, pharmacokinetic and pharmacodynamic considerations, methods of administration (bolus versus infusion), or specific modalities for mechanical fluid removal (ultrafiltration, intermittent hemodialysis, and continuous RRT). The reasons for fluid removal varied (Table 3). Further, some studies focused on fluid removal only, while others combined fluid removal with minimization of fluid intake (Table 3). Marked differences were also noted between the study protocols as well as the criteria for comparator and usual care. Importantly, the application of usual care does not exclude the use of diuretics, ultrafiltration or RRT should clear indications for these interventions arise. In some of the RCTs, patients randomized to usual care received larger doses of diuretics or RRT more often than patients in the active intervention arm [30]. In fact, the intervention and the comparator are potentially overlapping strategies distinguished mostly by the intent of actively accelerating a process that may occur later, either with a medical intervention or spontaneously.

Review of the literature also confirmed heterogeneity in terminology and clinical practice of fluid management and assessment of fluid status [60, 65, 66]. The majority of studies did not attempt to use specific criteria to determine readiness for fluid removal or safety indicators when to stop fluid removal [60]. Chen et al. postponed initiation of a conservative fluid-management strategy until patients were demonstrated to be volume unresponsive, but most other studies did not comment on readiness for fluid removal [25]. A previous systematic review of 49 studies in patients with adult respiratory distress syndrome, sepsis, or systemic inflammatory response syndrome revealed that the majority of studies had not attempted to use specific criteria to determine readiness for conservative fluid management or fluid removal [66]. In the view of the panel, this is an important point. Active fluid removal should only be considered in patients who do not need fluid resuscitation. Further, when depleting the plasma volume, it is essential that refilling of plasma from the interstitium takes place. However, the plasma 'capillary refill rate' is highly variable among individuals, and may be decreased in conditions associated with vasoplegia, endothelial dysfunction, increased capillary permeability, and low intravascular oncotic pressure. To date, it is not possible to measure capillary refill rate in routine clinical practice.

Also, during active fluid removal, redistribution of blood from unstressed to stressed volume is essential but may be hampered in conditions associated with low vasomotor tone. Finally, impaired systolic or diastolic function may impact patients' ability to tolerate rapid fluid withdrawal.

The process of fluid removal requires an understanding of the different fluid compartments, precise assessment of fluid status, regular monitoring, identification of safety limits, and determination of criteria for discontinuation, and needs to be individualized. All these aspects are very important in clinical practice and described in detail in many review papers [5, 41, 44, 60, 67–72] but out of scope of this evidence-based guideline.

Our recommendations apply to patients who are beyond the active resuscitation phase and no longer need fluid resuscitation. We did not include the GO NEUTRAL study as it was considered to be performed in the resuscitative phase as illustrated by the use of high-dose norepinephrine at time of randomization [73]. The trial provides some evidence that active control of fluid balance by mechanical fluid removal in patients receiving continuous RRT coupled with minimizing fluid intake using a functional hemodynamic protocol is feasible in the early resuscitation phase in patients with acute circulatory shock and severe AKI. Further research is needed to investigate whether the protocol is indeed safe and whether short-term changes in cumulative fluid balance during the active resuscitation phase translate into improved clinical outcomes [74].

Conclusions

These guidelines include 3 evidence-based recommendations regarding the practice of fluid removal during the de-escalation phase in patients who no longer need fluid resuscitation. The panel issued a conditional

recommendation in favor of diuretics over usual care and a recommendation against the routine use of ultrafiltration or extracorporeal fluid removal in patients without other indications for RRT. Important knowledge gaps remain. There is an urgent need for more research in individualized fluid management [75] and standardization of the terminology.

Supplementary Information
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Data availability statement
Data will be available at request.

Declarations

Conflicts of interest
MO received research funding from Baxter and Biomerieux (paid to institution). AA received research funding grant from Grifols (paid to institution). CI received honoraria for lectures and speakers for educational events. CAP report grants from B. Braun Medical AG, CSEM AG outside of the submitted work. The funding was paid into departmental funds. MM is co-founder, past-President, and current Treasurer of WSACS (The Abdominal Compartment Society, http://www.wsacs.org). He is member of the medical advisory Board of Pulsion Medical Systems (now fully part of Getinge group), Sentinel Medical, Maltron, and Baxter. He consults for BBraun, Becton Dickinson, Fresenius Kabi, Grifols, Lexin, Spiegelberg, Medtronic, MedCaptain, and Holtech Medical, and received speaker's fees from PeerVoice. He holds stock options for Sentinel, Serenno, and Potrero. He is co-founder and President of the International Fluid Academy (IFA). The IFA (http://www.fluidacademy.org) is integrated within the not-for-profit charitable organization iMERiT, International Medical Education and Research Initiative, under Belgian law. DdB has received honoraria for lectures from Edwards Lifesciences, Philips, AOP Health, Viatris, and Pharmazz. MC provides consultancy for GE Healthcare, Edwards Lifesciences, and Directed Systems. All other authors have nothing to declare.

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References

1. Messina A, Bakker J, Chew M, De Backer D, Hamzaoui O, Hernandez G, Myatra SN, Monnet X, Ostermann M, Pinsky M et al (2022) Pathophysiology of fluid administration in critically ill patients. Intensive Care Med Exp 10(1):46
2. Vincent JL, De Backer D (2013) Circulatory shock. N Engl J Med 369(18):1726–1734
3. White KC, Serpa-Neto A, Hurford R, Clement P, Laupland KB, Ostermann M, Sanderson B, Gatton M, Bellomo R (2024) How a positive fluid balance develops in acute kidney injury: a binational, observational study. J Crit Care 82:154809
4. Zhang J, Crichton S, Dixon A, Seylanova N, Peng ZY, Ostermann M (2019) Cumulative fluid accumulation is associated with the development of acute kidney injury and non-recovery of renal function: a retrospective analysis. Crit Care 23(1):392
5. Pfortmueller CA, Dabrowski W, Wise R, van Regenmortel N, Malbrain M (2024) Fluid accumulation syndrome in sepsis and septic shock: pathophysiology, relevance and treatment-a comprehensive review. Ann Intensive Care 14(1):115
6. Arabi YM, Belley-Cote E, Carsetti A, De Backer D, Donadello K, Juffermans NP, Hammond N, Laake JH, Liu D, Maitland K et al (2024) European Society of Intensive Care Medicine clinical practice guideline on fluid therapy in adult critically ill patients. Part 1: the choice of resuscitation fluids. Intensive Care Med 50(6):813–831
7. Cecconi M, Kesecioglu J, Azoulay E (2021) Diversity and inclusivity: the way to multidisciplinary intensive care medicine in Europe. Intensive Care Med 47(5):598–601
8. Alhazzani W, Lewis K, Jaeschke R, Rochwerg B, Møller MH, Evans L, Wilson KC, Patel S, Coopersmith CM, Cecconi M et al (2018) Conflicts of interest disclosure forms and management in critical care clinical practice guidelines. Intensive Care Med 44(10):1691–1698

9. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, Alderson P, Glasziou P, Falck-Ytter Y, Schünemann HJ (2011) GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 64(4):395–400
10. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7(3):177–188
11. DerSimonian R, Laird N (2015) Meta-analysis in clinical trials revisited. Contemp Clin Trials 45(Pt A):139–145
12. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327(7414):557–560
13. Santesso N, Glenton C, Dahm P, Garner P, Akl EA, Alper B, Brignardello-Petersen R, Carrasco-Labra A, De Beer H, Hultcrantz M et al (2020) GRADE guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. J Clin Epidemiol 119:126–135
14. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, DeBeer H et al (2011) GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 64(4):383–394
15. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S et al (2011) GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 64(4):401–406
16. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, Montori V, Akl EA, Djulbegovic B, Falck-Ytter Y (2011) GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). J Clin Epidemiol 64(4):407–415
17. How to GRADE the evidence: imprecision. http://training.cochrane.org/resource/how-grade-evidence-imprecision
18. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, Devereaux PJ, Montori VM, Freyschuss B, Vist G et al (2011) GRADE guidelines 6. Rating the quality of evidence–imprecision. J Clin Epidemiol 64(12):1283–1293
19. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, Alonso-Coello P, Falck-Ytter Y, Jaeschke R, Vist G et al (2011) GRADE guidelines: 8. Rating the quality of evidence–indirectness. J Clin Epidemiol 64(12):1303–1310
20. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, Alonso-Coello P, Glasziou P, Jaeschke R, Akl EA et al (2011) GRADE guidelines: 7. Rating the quality of evidence–inconsistency. J Clin Epidemiol 64(12):1294–1302
21. Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, Alonso-Coello P, Djulbegovic B, Atkins D, Falck-Ytter Y et al (2011) GRADE guidelines: 5. Rating the quality of evidence–publication bias. J Clin Epidemiol 64(12):1277–1282
22. Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, Atkins D, Kunz R, Montori V, Jaeschke R et al (2013) GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. J Clin Epidemiol 66(2):151–157
23. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, Nasser M, Meerpohl J, Post PN, Kunz R et al (2013) GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol 66(7):719–725
24. Andrews JC, Schünemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, Rind D, Montori VM, Brito JP, Norris S et al (2013) GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol 66(7):726–735
25. Chen C, Kollef MH (2015) Targeted fluid minimization following initial resuscitation in septic shock: a pilot study. Chest 148(6):1462–1469
26. Bagshaw SM, Gibney RTN, Kruger P, Hassan I, McAlister FA, Bellomo R (2017) The effect of low-dose furosemide in critically ill patients with early acute kidney injury: a pilot randomized blinded controlled trial (the SPARK study). J Crit Care 42:138–146
27. Berthelsen RE, Perner A, Jensen AK, Rasmussen BS, Jensen JU, Wiis J, Behzadi MT, Bestle MH (2018) Forced fluid removal in intensive care patients with acute kidney injury: the randomised FFAKI feasibility trial. Acta Anaesthesiol Scand 62(7):936–944
28. Cinotti R, Lascarrou JB, Azais MA, Colin G, Quenot JP, Mahé PJ, Roquilly A, Gaultier A, Asehnoune K, Reignier J (2021) Diuretics decrease fluid balance in patients on invasive mechanical ventilation: the randomized-controlled single blind, IRIHS study. Crit Care 25(1):98
29. Silversides JA, McMullan R, Emerson LM, Bradbury I, Bannard-Smith J, Szakmany T, Trinder J, Rostron AJ, Johnston P, Ferguson AJ et al (2022) Feasibility of conservative fluid administration and deresuscitation compared with usual care in critical illness: the Role of Active Deresuscitation After Resuscitation-2 (RADAR-2) randomised clinical trial. Intensive Care Med 48(2):190–200
30. Vaara ST, Ostermann M, Bitker L, Schneider A, Poli E, Hoste E, Fierens J, Joannidis M, Zarbock A, van Haren F et al (2021) Restrictive fluid management versus usual care in acute kidney injury (REVERSE-AKI): a pilot randomized controlled feasibility trial. Intensive Care Med 47(6):665–673
31. Mekontso Dessap A, Roche-Campo F, Kouatchet A, Tomicic V, Beduneau G, Sonneville R, Cabello B, Jaber S, Azoulay E, Castanares-Zapatero D et al (2012) Natriuretic peptide-driven fluid management during ventilator weaning: a randomized controlled trial. Am J Respir Crit Care Med 186(12):1256–1263
32. Cantarovich F, Rangoonwala B, Lorenz H, Verho M, Esnault VL (2004) High-dose furosemide for established ARF: a prospective, randomized, double-blind, placebo-controlled, multicenter trial. Am J Kidney Dis 44(3):402–409
33. Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, deBoisblanc B, Connors AF Jr, Hite RD, Harabin AL (2006) Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 354(24):2564–2575
34. Hamishehkar H, Sanaie S, Fattahi V, Mesgari M, Mahmoodpoor A (2017) The effect of furosemide on the level of neutrophil gelatinase-associated lipocalin in critically hospitalized patients with acute kidney injury. Indian J Crit Care Med 21(7):442–447
35. Mitchell JP, Schuller D, Calandrino FS, Schuster DP (1992) Improved outcome based on fluid management in critically ill patients requiring pulmonary artery catheterization. Am Rev Respir Dis 145(5):990–998
36. Semler MW, Janz DR, Casey JD, Self WH, Rice TW (2020) Conservative fluid management after sepsis resuscitation: a pilot randomized trial. J Intensive Care Med 35(12):1374–1382
37. Wichmann S, Schønemann-Lund M, Perner A, Itenov TS, Lange T, Gluud C, Berthelsen RE, Brøchner AC, Wiis J, Bestle MH (2023) Goal-directed fluid removal with furosemide versus placebo in intensive care patients with fluid overload: a randomised, blinded trial (GODIF trial-First version). Acta Anaesthesiol Scand 67(4):470–478
38. Sakr Y, Rubatto Birri PN, Kotfis K, Nanchal R, Shah B, Kluge S, Schroeder ME, Marshall JC, Vincent JL (2017) Higher fluid balance increases the risk of death from sepsis: results from a large international audit. Crit Care Med 45(3):386–394
39. Hofer DM, Ruzzante L, Waskowski J, Messmer AS, Pfortmueller CA (2024) Influence of fluid accumulation on major adverse kidney events in critically ill patients—an observational cohort study. Ann Intensive Care 14(1):52
40. Kuhnert S, Sommerlad J, Gall H, Weder MM, Wolff M, Eberle S, Sander M, Reichert M, Koch C, Askevold I et al (2024) Postoperative fluid accumulation is associated with underestimation of AKI severity in lung transplant recipients. Clin Transplant 38(9):e15457
41. De Backer D, Ostermann M, Monnet X (2023) The nuts and bolts of fluid de-escalation. Intensive Care Med 49(9):1120–1122
42. Hall A, Crichton S, Dixon A, Skorniakov I, Kellum JA, Ostermann M (2020) Fluid removal associates with better outcomes in critically ill patients receiving continuous renal replacement therapy: a cohort study. Crit Care 24(1):279
43. Murugan R, Kerti SJ, Chang CH, Gallagher M, Clermont G, Palevsky PM, Kellum JA, Bellomo R (2019) Association of net ultrafiltration rate with mortality among critically ill adults with acute kidney injury receiving continuous venovenous hemodiafiltration: a secondary analysis of the randomized evaluation of normal vs augmented level (RENAL) of renal replacement therapy trial. JAMA Netw Open 2(6):e195418
44. De Backer D, Cecconi M, Chew MS, Hajjar L, Monnet X, Ospina-Tascón GA, Ostermann M, Pinsky MR, Vincent JL (2022) A plea for personalization of the hemodynamic management of septic shock. Crit Care 26(1):372
45. Lee TH, Kuo G, Chang CH, Huang YT, Yen CL, Lee CC, Fan PC, Chen JJ (2021) Diuretic effect of co-administration of furosemide and albumin in comparison to furosemide therapy alone: an updated systematic review and meta-analysis. PLoS ONE 16(12):e0260312
46. Morsch C, Thomé FS, Balbinotto A, Guimarães JF, Barros EG (2011) Health-related quality of life and dialysis dependence in critically ill patient survivors of acute kidney injury. Ren Fail 33(10):949–956

47. Trawalé JM, Paradis V, Rautou PE, Francoz C, Escolano S, Sallée M, Durand F, Valla D, Lebrec D, Moreau R (2010) The spectrum of renal lesions in patients with cirrhosis: a clinicopathological study. Liver Int 30(5):725–732
48. Mikkelsen ME, Christie JD, Lanken PN, Biester RC, Thompson BT, Bellamy SL, Localio AR, Demissie E, Hopkins RO, Angus DC (2012) The adult respiratory distress syndrome cognitive outcomes study: long-term neuropsychological function in survivors of acute lung injury. Am J Respir Crit Care Med 185(12):1307–1315
49. Ostermann M, Awdishu L, Legrand M (2024) Using diuretic therapy in the critically ill patient. Intensive Care Med 50(8):1331–1334
50. Che ML, Yan YC, Zhang Y, Gu Y, Wang NS, Chen N, Mao PJ, Zhang JY, Ding XQ, Yuan WJ et al (2009) Analysis of drug-induced acute renal failure in Shanghai. Zhonghua Yi Xue Za Zhi 89(11):744–749
51. Bell R, Mandalia R (2022) Diuretics and the kidney. BJA Educ 22(6):216–223
52. Testani JM, Chen J, McCauley BD, Kimmel SE, Shannon RP (2010) Potential effects of aggressive decongestion during the treatment of decompensated heart failure on renal function and survival. Circulation 122(3):265–272
53. Rosner MH, Ostermann M, Murugan R, Prowle JR, Ronco C, Kellum JA, Mythen MG, Shaw AD (2014) Indications and management of mechanical fluid removal in critical illness. Br J Anaesth 113(5):764–771
54. Ellison DH (2001) Diuretic therapy and resistance in congestive heart failure. Cardiology 96(3–4):132–143
55. Sansom B, Tonkin-Hill G, Kalfas S, Park S, Presneill J, Bellomo R (2022) The relationship between commencement of continuous renal replacement therapy and urine output, fluid balance, mean arterial pressure and vasopressor dose. Crit Care Resusc 24(3):259–267
56. Bisht H, Tripathi A, Arya A, Konat A, Patel D, Godhani D, Kamaria R, Shah P, Chudasama G, Jain P et al (2023) Ultrafiltration in heart failure: a review. Cureus 15(6):e39933
57. Bart BA, Goldsmith SR, Lee KL, Givertz MM, O'Connor CM, Bull DA, Redfield MM, Deswal A, Rouleau JL, LeWinter MM et al (2012) Ultrafiltration in decompensated heart failure with cardiorenal syndrome. N Engl J Med 367(24):2296–2304
58. Jamison DT, Gelband H, Horton S, Jha P, Laxminarayan R, Mock CN, Nugent R (2017) Disease control priorities: improving health and reducing poverty. Washington (DC): The International Bank for Reconstruction and Development/The World Bank © 2018 International Bank for Reconstruction and Development/The World Bank
59. Villeneuve PM, Clark EG, Sikora L, Sood MM, Bagshaw SM (2016) Health-related quality-of-life among survivors of acute kidney injury in the intensive care unit: a systematic review. Intensive Care Med 42(2):137–146
60. Malbrain M, Martin G, Ostermann M (2022) Everything you need to know about deresuscitation. Intensive Care Med 48(12):1781–1786
61. Pfortmueller CA, Dabrowski W, Malbrain M (2023) Fluid de-resuscitation in critical illness—a journey into uncertain territory. J Crit Care 76:154249
62. Lintz VC, Vieira RA, Carioca FL, Ferraz IS, Silva HM, Ventura AMC, de Souza DC, Brandão MB, Nogueira RJN, de Souza TH (2024) Fluid accumulation in critically ill children: a systematic review and meta-analysis. EClinicalMedicine 74:102714
63. White KC, Bellomo R, Laupland KB, Gatton ML, Ostermann M, McIlroy P, Luke S, Garrett P, Tabah A, Whebell S et al (2025) Predicting a strongly positive fluid balance in critically ill patients with acute kidney injury: a multicentre, international study. J Crit Care 87:155016
64. Silversides JA, McAuley DF, Blackwood B, Fan E, Ferguson AJ, Marshall JC (2020) Fluid management and deresuscitation practices: a survey of critical care physicians. J Intensive Care Soc 21(2):111–118
65. White KC, Laupland KB, Ostermann M, Neto AS, Gatton ML, Hurford R, Clement P, Sanderson B, Bellomo R (2024) Current fluid management practice in critically ill adults on continuous renal replacement therapy: a binational, observational study. Blood Purif 53(8):624–633
66. Silversides JA, Major E, Ferguson AJ, Mann EE, McAuley DF, Marshall JC, Blackwood B, Fan E (2017) Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis. Intensive Care Med 43(2):155–170
67. Malbrain M, Caironi P, Hahn RG, Llau JV, McDougall M, Patrão L, Ridley E, Timmins A (2023) Multidisciplinary expert panel report on fluid stewardship: perspectives and practice. Ann Intensive Care 13(1):89
68. Ostermann M, Auzinger G, Grocott M, Morton-Bailey V, Raphael J, Shaw AD, Zarbock A (2024) Perioperative fluid management: evidence-based consensus recommendations from the international multidisciplinary PeriOperative Quality Initiative. Br J Anaesth 133(6):1263–1275
69. Selewski DT, Barhight MF, Bjornstad EC, Ricci Z, de Sousa TM, Akcan-Arikan A, Goldstein SL, Basu R, Bagshaw SM (2024) Fluid assessment, fluid balance, and fluid overload in sick children: a report from the Pediatric Acute Disease Quality Initiative (ADQI) conference. Pediatr Nephrol 39(3):955–979
70. Reis T, Ronco F, Ostermann M (2023) Diuretics and ultrafiltration in heart failure. Cardiorenal Med 13(1):56–65
71. De Backer D, Aissaoui N, Cecconi M, Chew MS, Denault A, Hajjar L, Hernandez G, Messina A, Myatra SN, Ostermann M et al (2022) How can assessing hemodynamics help to assess volume status? Intensive Care Med 48(10):1482–1494
72. Ostermann M, Liu K, Kashani K (2019) Fluid management in acute kidney injury. Chest 156(3):594–603
73. Bitker L, Dupuis C, Pradat P, Deniel G, Klouche K, Mezidi M, Chauvelot L, Yonis H, Baboi L, Illinger J et al (2024) Fluid balance neutralization secured by hemodynamic monitoring versus protocolized standard of care in patients with acute circulatory failure requiring continuous renal replacement therapy: results of the GO NEUTRAL randomized controlled trial. Intensive Care Med 50(12):2061–2072
74. Murugan R, Prowle J, Beaubien-Souligny W (2024) Protocolized fluid balance neutralization during continuous renal replacement therapy. Intensive Care Med 50(12):2141–2143
75. De Backer D, Deutschman CS, Hellman J, Myatra SN, Ostermann M, Prescott HC, Talmor D, Antonelli M, Pontes Azevedo LC, Bauer SR et al (2024) Surviving sepsis campaign research priorities 2023. Crit Care Med 52(2):268–296